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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
09/027,205	02/20/98	JUNE	GIN-005

C
EXAMINER

000959
LAHIVE & COCKFIELD
28 STATE STREET
BOSTON MA 02109

HM12/0927

ART UNIT	PAPER NUMBER
1644	9

DATE MAILED: 09/27/99

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 7/6/99

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 1-54 is/are pending in the application.
Of the above, claim(s) 3,5-7, 16-54 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☑ Claim(s) 1,2,4, 8-15 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☑ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). 4
☐ Interview Summary, PTO-413
☑ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

★ U.S. GPO: 1998-404-496/40517

DETAILED ACTION

1. Applicant's submission, filed 7/6/99 (Paper No. 7), is in compliance with the Sequence Rules.

2. Applicant's election of Group I and the species anti-CD28 antibody in Paper No. 7 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818).
Claims 1-2, 4 and 8-15, as they read on upregulating HIV-1 fusion cofactor expression are under consideration in the instant application.

Claims 3, 5-7 and 16-54 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected inventions and species.

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Applicant should restrict the title to the claimed invention, that is, downregulating HIV-1 fusion cofactor expression.

4. Drawings comply with 37 CFR 1.84. Please see the enclosed form PTO-948.

5. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Applicant is required to identify the nucleotide and amino acid sequences in the specification with SEQ. ID NOS.

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate corrections are required, if necessary.

6. The following is a quotation of the first paragraph of 35 U.S.C. § 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 2, 4 and 8-15 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

There is insufficient guidance and direction in the specification as filed on how to increase HIV-1 cofactor expression (e.g. CCR5) on the surface of a T cell either in vitro or in vivo, or to increase HIV-1 fusion cofactor expression on the surface of a T cell in a practical manner either in vitro or in vivo. Except for cryptic sentences in the Summary of the Invention (see page 2); there does not appear to any further disclosure of such methods to increase HIV-1 fusion cofactor expression. Furthermore, it is noted that the elected species of anti-CD28 antibodies that are employed to stimulate accessory molecules on the surface of T cells result in downregulating HIV-1 fusion cofactor expression (see Summary of the Invention; Uses of the Invention).

In addition, given that the specification discloses that the activation via costimulatory molecules (e.g. CD28) leads to downregulating HIV cofactor expression, which is a desirable goal; it is not readily apparent how the skilled artisan would use the claimed methods to achieve an undesirable endpoint, that is, increasing HIV-1 fusion cofactor expression which would result in increased HIV transmission. Again, there is insufficient and guidance in the specification as filed for how the skilled artisan would increase HIV-1 cofactor expression (e.g. CCR5) on the surface of a T cell either in vitro or in vivo and for what desired endpoint would the skilled artisan would carry out such methods.

Furthermore, there is insufficient direction and guidance as to ingredients or elements, method steps and endpoints in order to carry out the claimed in vitro and in vivo methods of increasing HIV-1 fusion cofactor expression by stimulating a costimulatory molecule, including CD28.

Given that it has been well known in the art that retroviral infections in general, and HIV infections in particular, are refractory to anti-viral therapies; it is not clear how one skilled in the art would use the claimed invention with a reasonable expectation of success and without undue experimentation to achieve the opposite endpoint, i.e. upregulating HIV-1 fusion cofactor expression leading to increase HIV transmission and infection. The specification does not teach how to extrapolate data obtained from in vitro assays which appear to be primarily drawn to the downregulating HIV-1 fusion cofactor expression, particularly of M-tropic viruses to the development of either effective or predictive in vitro or in vivo methods to increase HIV-1 fusion cofactor expression, commensurate in scope with the claimed invention. Again, the claimed / elected methods appear to be drawn or to encompass methods of increasing HIV infection and transmission in vivo. It is not clear why the skilled artisan would practice the claimed methods in vivo, wherein the claimed methods appear to be detrimental to the health of patients; in the absence of evidence to the contrary.

8. Claims 1, 2, 4, and 8-15 are rejected under 35 U.S.C. § 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) HIV-1 fusion cofactor (claims 1, 2 and 8-15):

The instant claims are indefinite in the recitation of "HIV-1 fusion cofactor" because the characteristics of the "HIV-1 fusion cofactor(s)" are not known. This language is vague and indefinite because the metes and bounds of said "HIV-1 fusion cofactor(s)" are not clearly delineated and it is not apparent from the disclosure which particular "cofactor(s)" are being referred to; other than CCR5. Applicant has not provided sufficient biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, etc.) that distinctly identifies the "HIV-1 fusion cofactor(s)" encompassed by the claimed invention. While the name itself may have some notion of the activity of the protein, there is nothing in the claims which distinctly claims the "HIV-1 fusion cofactor". The recitation of "HIV-1 fusion cofactor" fails to distinctly claim what that "cofactor" is and what it is made up of.

There is insufficient direction or guidance provided to assist one skilled in the art in the selection of any "HIV-1 fusion cofactor" nor is there sufficient evidence provided that any such "HIV-1 fusion cofactor(s)" could be used in a practical manner either in vitro or in vivo as subject to the manipulation of an accessory molecule such as CD28 on the surface of a T cell. It would require undue experimentation to investigate all such possible "HIV-1 cofactor(s)" without more explicit guidance from the disclosure. Applicant has failed to enable or provide sufficient guidance and direction to determine the extent of "HIV-1 fusion cofactor(s)", nor is there is sufficient direction and guidance how to use any such "HIV-1 fusion cofactor(s)" in the claimed methods, including their nexus to costimulatory molecules such as CD28. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. It appears that undue experimentation would be required of one skilled in the art to practice the claimed methods with any "HIV-1 fusion cofactor(s)" commensurate in scope with the claimed invention using the teaching of the specification. Without such guidance, targeting costimulatory signals to increase HIV-1 fusion cofactor expression would be unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue

Applicant's limiting the "HIV-1 fusion cofactor" to CCR5, as the only HIV-1 fusion cofactor disclosed in the specification as filed, would obviate this 35 USC, 112,first and second paragraph, rejection.

B) Accessory molecule (claims 1, 2, 4, 8-15):

The instant claims are indefinite in the recitation of "accessory molecule" because the characteristics of the "accessory molecule(s) are ambiguous and unclear. This language is vague and indefinite because the metes and bounds of said "accessory molecule(s)" are not clearly delineated. Applicant has not provided sufficient biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, etc.) that distinctly identifies the "accessory molecule(s)" encompassed by the claimed invention. While the name itself may have some notion of the activity of the protein, there is nothing in the claims which distinctly claims the "accessory molecule(s)". The recitation of "accessory molecule(s)" fails to distinctly claim what that "accessory molecule(s)" is and what it is made up of. While the name itself may have some notion of the activity of the protein, there is nothing in the claims which distinctly claims the "accessory molecule(s)".

There is insufficient direction or guidance provided to assist one skilled in the art in the selection of any "accessory molecule" nor is there sufficient evidence provided that manipulating any such "accessory molecule" could be used in a practical manner either in vitro or in vivo to decrease HIV-1 fusion cofactor expression. It would require undue experimentation to investigate all such "accessory molecule(s)" which are expressed on T cells and, in turn, affect (or downregulate) HIV-1 fusion cofactor expression. Applicant has failed to enable or provide sufficient guidance and direction to determine the extent of "accessory molecule(s)" encompassed by the claimed methods, nor is there is sufficient direction and guidance how to manipulate any such "accessory molecule" in the claimed methods to increase HIV-1 fusion cofactor expression. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. It appears that undue experimentation would be required of one skilled in the art to practice the claimed methods with any "accessory molecule(s)" commensurate in scope with the claimed invention using the teaching of the specification. Without such guidance, targeting costimulatory signals to increase HIV-1 fusion cofactor expression would be unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue

Applicant is invited to consider limiting the accessory molecules to certain members of the B7:CD28 pathway that are expressed on T cells.

C) An agent which interacts with the accessory molecule (claim 13)

The instant claims are indefinite in the recitation of "agent" because the characteristics of the "agent(s)" are not known. This language is vague and indefinite because the metes and bounds of said "agent(s)" are not clearly delineated and it is not apparent from the disclosure which particular "agent(s)" are being referred to. Applicant has not provided sufficient biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, etc.) that distinctly identifies the "agent(s)" encompassed by the claimed invention. The recitation of "an agent which interacts with the accessory molecule" fails to distinctly claim what that "agent(s)" is and what it is made up of. While the phrase "an agent which interacts with the accessory molecule" itself may have some notion of the activity of the "agent", there is nothing in the claims which distinctly claims the "agent(s)".

There is insufficient direction or guidance provided to assist one skilled in the art in the selection of any "agent which interacts with the accessory molecule"HIV-1 fusion cofactor", which results in the upregulation of HIV-1 fusion cofactor; nor is there sufficient evidence provided that any such "agent(s)" could be used in a practical manner either in vitro or in vivo to achieve the claimed endpoint. It would require undue experimentation to investigate all such possible "agent(s)" without more explicit guidance from the disclosure. Applicant has failed to enable or provide sufficient guidance and direction to determine the extent of "agent(s)", nor is there is sufficient direction and guidance how to use any such "agent(s)" in the claimed methods, including their nexus to costimulatory molecules such as CD28. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. It appears that undue experimentation would be required of one skilled in the art to practice the claimed methods with any "agent(s)" commensurate in scope with the claimed invention using the teaching of the specification. Without such guidance, targeting costimulatory signals to increase HIV-1 fusion cofactor expression would be unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

D) The applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter.

9. Claims 1, 2, 4, 8-15 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) The claimed methods do not set forth clear, distinct and positive process steps, including providing the appropriate reagents/elements to carry out the claimed methods, including a resolution or correlating step that clearly relates to the preamble of the claim (claims 1, 2, 4, 8-15).

B) Claim 1, 2, 4 and 11-15 are indefinite in its recitation of "modulating" because it is ambiguous as to the direction (positive or negative) or degree of said modulating. Furthermore, the claims are indefinite in that they recite non-elected limitations (e.g. modulating as it reads on downregulating) and does not clearly recited the elected invention, drawn to increasing HIV-1 fusion cofactor expression.

C) The applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for

11. Claims 1, 2, 4, 8-10, 12-15 are rejected under 35 U.S.C. § 102(b) as being anticipated by Smithgall et al. (AIDS Research and Human Retroviruses 11: 885 - 892, 1995; 1449). Smithgall et al. Teach costimulation of T cells with CD28-specific antibodies, which modulates HIV infection and replication in vitro. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods, which use the CD28-specific antibodies to treat T cell antibodies, resulting in increased virus replication, encompassed by the claimed methods. Also, see Ex parte Novitski 26 USPQ 1389 (BPAI 1993).

12. Claims 1, 2, 4, 8-10, 12-15 are rejected under 35 U.S.C. § 102(b) as being anticipated by Pinchuk et al. (Immunity 1: 317 - 325, 1994; 1449). Pinchuk et al. teach costimulation of T cells with CD28-specific antibodies, which modulates HIV infection and replication in vitro. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods, which use the CD28-specific antibodies to treat T cell antibodies, resulting in increased virus replication, encompassed by the claimed methods. Also, see Ex parte Novitski 26 USPQ 1389 (BPAI 1993).

13. No claim is allowed.

It is noted that the claimed methods encompassing in vivo methods of upregulating HIV-1 fusion cofactor expression is held free of the prior art, given that the ordinary artisan would not be motivated to apply such methods to increase HIV infection and transmission in patients.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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September 22, 1999
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